

REMARKS

Claims 1-5, 7, 10-15, and 17-30 are currently pending in this application. Claims 1-5, 7, 10-15, and 17-30 stand rejected; claims 6, 16, 33, 34, 40, 41 and 44 are cancelled; and claims 8, 9, 31, 32, 35-39, 42, 43, and 45-48 are withdrawn. Applicants have amended claim 1 and request entry of that amendment and reconsideration of the outstanding rejections. Claim 23 is canceled without prejudice or disclaimer.

Amendments to the Claims

Applicants have amended claim 1 to replace the phrase "or preventing vasomotor symptoms" with the phrase "hot flushes, excessive perspiration or night sweats." Support for this amendment is found for example at paragraph [0078]. Applicant submits that no new matter is introduced by this amendment. Withdrawn claims 31 and 38 have been amended to remove a duplicated listing of a compound.

Applicant requests the entry of the amendment under 37 C.F.R. § 1.116(b) because the amendments to the claims either cancel claims, comply with requirements of form expressly set forth in a previous Office Action, or present the rejected claims in better form for consideration on appeal.

The Claimed Invention Pending Claims

The pending claims, as currently amended, are drawn to: (1) a method for treating hot flushes, excessive perspiration or night sweats in a subject in need thereof, comprising administering to the subject a composition comprising a therapeutically effective amount of at least one norepinephrine reuptake inhibitor, such as for example desipramine, or pharmaceutically acceptable salt thereof; (2) a method for treating hot flushes, excessive perspiration or night sweats in a subject in need thereof, comprising administering to the subject a composition comprising a therapeutically effective amount of at least one norepinephrine reuptake inhibitor, such as for example desipramine, and a serotonin reuptake inhibitor, such as fluoxetine; and (3) a method for treating hot flushes, excessive perspiration or night sweats in a subject in need thereof, comprising administering to the subject a composition comprising a therapeutically effective amount of at least one norepinephrine reuptake inhibitor, such as for example desipramine, and an $\alpha 2$ adrenergic antagonist, such as atipamezole.

Rejections under 35 USC § 112 ¶ 1 (Enablement)

Claims 1-5, 7, 10-15, and 17-30 stand rejected under 35 USC § 112 first paragraph for allegedly not providing enablement for a method of *preventing* vasomotor symptoms. Without conceding the merits of the rejection and solely for the purpose of expediting prosecution, Applicants amend claim 1 by deleting the phrase “or preventing.”

Since claims 2-5, 7, 10-15, and 17-30 depend directly or indirectly from claim 1, the amendment renders moot this enablement rejection for all of claims 1-5, 7, 10-15, and 17-30. Applicants request withdrawal of the rejection of these claims under 35 USC § 112 ¶ 1, enablement.

Rejections under 35 USC § 103(a)

Claims 1-5, 7, 23-30

Claims 1-5, 7, and 23-30 stand rejected under 35 USC § 103(a) as allegedly being unpatentable over Stearns, *Annals of Oncology*, Vol. 11, pp. 17-22, PTO-1449 (“Stearns”), and further in view of Janowsky *et al.*, *The Journal of Clinical Psychiatry*, Vol. 45, No. 10, Sec. 2, pp. 3-7, PTO-1449 (“Janowsky.”)

The Examiner cites Stearns as teaching:

- a. “vasomotor symptoms such as hot flashes ... [include the] sensation of heat accompanied by sweating, flushing, palpitations anxiety, irritability, panic attack ... [and] are also accompanied by co-existing symptoms, including depression, nervousness, agitation, insomnia, and inability to concentrate, which symptoms can also exacerbate hot flashes,” (Office action of 10/19/2007, p. 8, second paragraph, lines 1-6);
- b. SSRIs, such as paroxetine HCl, which are anti-depressants, might be effective in treating hot flashes; and
- c. the SSRI venlafaxine HCl was evaluated for treatment of hot flashes in andropausal males.

The Examiner admits that “Stearns does not specifically teach administration of ... a norepinephrine reuptake inhibitor such as desipramine,” and cites Janowsky as teaching that “desipramine is a novel antidepressant.”

The Examiner contends that it would have been obvious for one skilled in the art to administer a compound “such as desipramine ... for the treatment of depression, panic attack occurring as a co-symptom of hot flashes and/or menopause, as taught by Stearns ...”

Without conceding the merits of the rejection and solely for the purpose of expediting prosecution, Applicants amend claim 1 by replacing the phrase “vasomotor symptoms” with the phrase “hot flushes, excessive perspiration or night sweats.” This amendment does not contain new matter, since support for the amendment can be found at paragraphs [0057] and [0058]. Furthermore, the subject matter of the amendment is wholly contained within the umbrella of “vasomotor symptoms,” as defined in the specification at paragraph [0057].

Applicants traverse the rejection of claims 1-5, 7, and 23-30 under 35 USC 103(a) for allegedly being obvious over Stearns in view of Janowsky. Stearns teaches the *specific* use of SSRIs to treat hot flush, and not the use of antidepressants *in general* to treat hot flush. The theoretical basis for the use of SSRIs to treat hot flush is provided by Stearns at page 21, second paragraph, which is quoted below:

“The physiology of hot flashes is probably related to dysfunction of the thermoregulation set point [2]. Investigators have suggested that estrogen-withdrawal results in decreased levels of brain amines, such as serotonin [17]. This hypothesis might explain why estrogen withdrawal is associated not only with hot flashes, but also with alterations in sleep, anxiety and mood. Other investigators have demonstrated that blood levels of serotonin are diminished in menopausal women [18]. Moreover, estrogen replacement therapy appears to augment serotonergic activity [19]. The beneficial results observed in our study are consistent with the theory that SSRIs might be an effective therapy for hot flashes and associated perimenopausal symptoms.”

Stearns does not teach or suggest the use of norepinephrine reuptake inhibitors to treat hot flushes, excessive perspiration or night sweats, but rather teaches the use of the selective serotonin reuptake inhibitors paroxetine HCl and venlafaxine HCl to treat hot flush. The skilled artisan would not reasonably expect or predict that a norepinephrine reuptake inhibitor would be effective in relieving hot flushes, excessive perspiration or night sweats.

Janowsky merely identifies desipramine as having antidepressant activity. Thus, Janowsky fails to remedy the deficiency of Stearns.

In view of the foregoing amendment and arguments, Applicants submit that the combination of Stearns and Janowsky does not render claims 1-5, 7, and 23-30 obvious. Accordingly, Applicants request the Office to withdraw the rejection of claims 1-5, 7, and 23-30 under 35 U.S.C. § 103(a) over Stearns in view of Janowski.

Claim 22

Claim 22 stands rejected under 35 U.S.C. § 103(a) over Stearns in view of Janowski, and in further view of Gould, International Journal of Pharmaceutics, 33 (1986), pp. 201-217; PTO-892 ("Gould") The Examiner cites Gould for teaching hydrochloride salts of drugs. Applicants respectfully traverse the rejection.

Claim 22 depends from claim 1 and specifies that the pharmaceutically acceptable salt is an acid addition salt. Even if properly combinable (and applicants are not conceding that the references are properly combinable), applicants submit that Gould does not remedy the deficiencies of the combined teachings of Stearns and Janowsky. Therefore, the combination of Stearns, Janowsky, and Gould does not render claim 22 obvious. Accordingly, Applicants request the Office to withdraw the rejection of claim 22 under 35 U.S.C. 5 103(a) over Stearns in view of Janowski and Gould.

Claims 10-12

Claims 10-12 stand rejected under 35 U.S.C. 5 103(a) over Stearns in view of Janowsky and in further view of WO 99/44601 ("Hunter "). Applicants respectfully traverse the rejection.

Claims 10-12 depend from claim 1 and specify that the method further includes the administration of an SRI or a pharmaceutically acceptable salt thereof. Even if properly combinable (and Applicants are not conceding that the references are properly combinable), Applicants submit that Hunter does not remedy the deficiencies of the combined teachings of Stearns and Janowsky. Therefore, the combination of Stearns, Janowsky and Hunter does not render claims 10-12 obvious. Accordingly, Applicants request the Office to withdraw the rejection of claim 10 to 12 under 35 U.S.C. § 103(a) over Stearns in view of Janowsky in further view of Hunter.

Claims 13-15 and 17-21

Claims 13-15 and 17-21 stand rejected under 35 U.S.C. § 103(a) over Stearns in view of Janowsky in further view of French, Pharmac. Ther., Volume 68, Number 2, pages 175 to 208, 1995 ("French"). Applicants respectfully traverse the rejection.

Claims 3-15 and 17-21 depend from claim 1 and specify that the method further includes the administration of an adrenergic_{α2} receptor antagonist or a pharmaceutically acceptable salt thereof. Even if properly combinable (and applicants are not conceding that the references are properly combinable), applicants submit that French does not remedy the deficiencies of the combined teachings of Stearns and Janowsky. Therefore, the combination of the Stearns, Janowsky, and French does not render claims 3-15 and 17-21 obvious. Accordingly, applicants request the Office to withdraw the rejection of claims 3-15 and 17-21 under 35 U.S.C. 5 103(a) over Stearns reference in view of Janowsky in further view of French.

Double Patenting

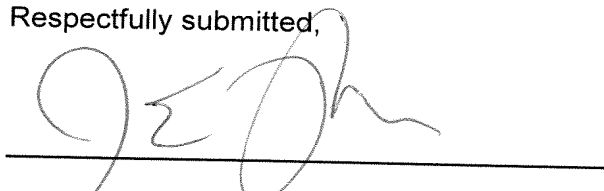
Claims 1-5, 7 and 22-30 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting over claims 1, 4-6 and 13-22 of copending U.S. Application No. 10/685,974. Applicants request that this rejection be held in abeyance until the identification of otherwise allowable subject matter.

Claims 1-5, 7, 13-17, 19 and 22-30 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting over claims 1-12 and 15-19 of copending U.S. Application No. 10/962,897. Applicants request that this rejection be held in abeyance until the identification of otherwise allowable subject matter.

CONCLUSION

In view of the foregoing, Applicant believes that all rejections have been overcome and claims 1-3 and 21-37 are in a condition for allowance. The Examiner is invited to call the undersigned agent to discuss any remaining issues.

Respectfully submitted,

A handwritten signature in dark ink, appearing to read 'J. E. Zahner', is written over a horizontal line.

Joseph E. Zahner
Agent for Applicant
Reg. No. 48,224

Wyeth
Patent Law Department
Five Giralda Farms
Madison, NJ 07940
Tel. No. (973) 660-6613
Fax. No. (973) 660-7151